

by **TANVIR SINGH, MD; KRISTI WILLIAMS, MD**

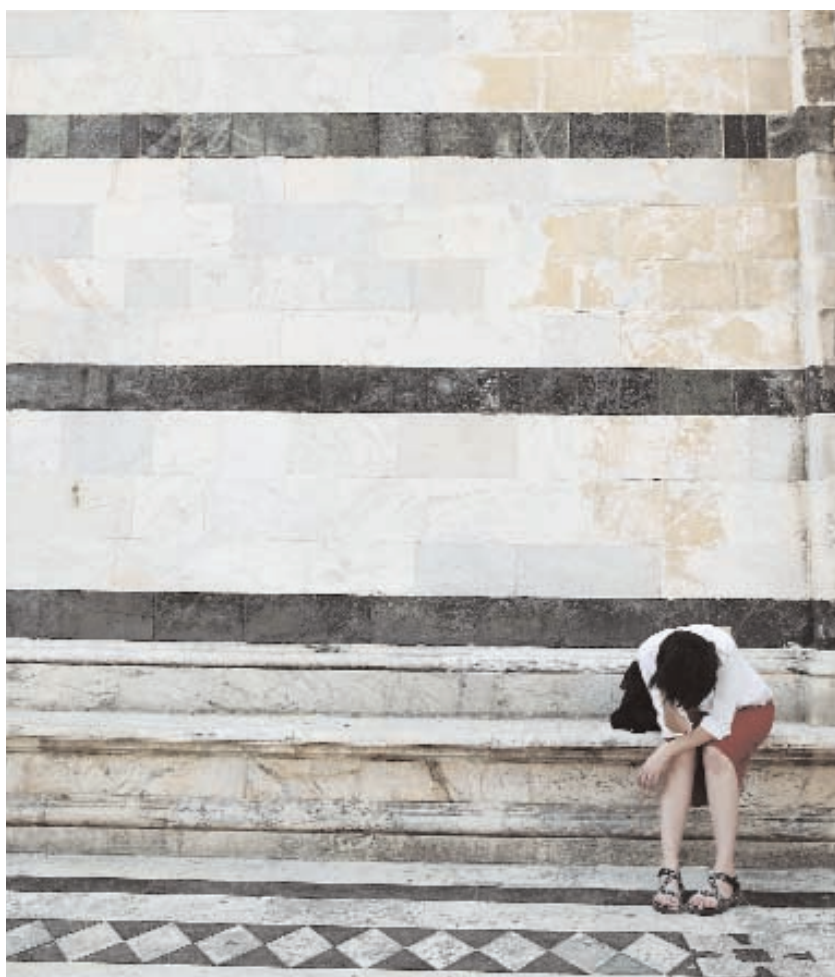
Dr. Singh is a resident and Dr. Williams is Associate Professor and Residency Program Director—Both from Medical University of Ohio, Department of Psychiatry, Toledo, Ohio.

Atypical Depression

DISCLOSURE: Dr. Williams is on the speakers bureau of Wyeth Pharmaceuticals.

ABSTRACT

The authors conducted Pubmed searches to examine the epidemiological characteristics, symptoms, association with bipolar disorder, personality and temperament features, biology, and pharmacotherapy response of atypical depression and significance of current knowledge about this subtype of depression in treatment planning. Atypical depression has a high prevalence rate, starts early in life, tends to last longer, is more likely to occur in people with bipolar disorder, has high comorbidity of anxiety disorders, carries more risk of suicidal behavior, and has distinct personality psychopathology and biological traits. Atypical depression is an important specifier with significance in terms of predicting clinical course of depression, and hence in treatment planning and service use.



ADDRESS CORRESPONDENCE TO:

Tanvir Singh, MD, Medical University of Ohio, Toledo, 3130 Glendale Ave., Toledo, OH 43614

Phone: (419) 383-5659; E-mail: tsingh@meduhio.edu

Key Words: Atypical depression, epidemiology, pharmacotherapy

INTRODUCTION

Several attempts have been made to categorize subtypes of depression that would predict response to antidepressant treatment.¹ Atypical depression as a separate diagnosis was introduced primarily because medication trials clearly showed such patients responded better to monoamine oxidase inhibitors (MAOIs) compared to tricyclic antidepressants (TCAs).²⁻⁵

The publication of the *Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition* in 1994 heralded the introduction of the term *atypical depression* in clinical psychiatry. West and Daley in 1959⁶ had initially used this term based on the unique symptom profile of reversed vegetative symptoms and hysterical personality traits in certain depressed patients.

- B. Two or more of the following features, present for most of the time, for at least two weeks:
1. Increased appetite
 2. Increased sleep
 3. Leadened paralysis (i.e., heavy, leaden feelings in arms or legs)
 4. Interpersonal rejection sensitivity (not limited to episodes of mood disturbance) resulting in significant social or occupational impairment
- C. Criteria are not met for melancholic or catatonic features of depression.

The introduction of SSRIs as antidepressants initially resulted in decrease of the interest in criteria of atypical depression, mainly because SSRIs were thought to be equally or more effective for symptoms of both atypical and nonatypical

We also will use current knowledge to examine the significance of this specifier with regard to management and treatment planning of depression.

METHODS

MEDLINE and PsycINFO searches of literature were performed to examine the significance of atypical depression as a specifier of depression. Search terms included *atypical depression* and *depression with atypical features*.

EPIDEMIOLOGY

Atypical depression is the most common form of depression seen in outpatient clinics in psychiatry.⁹ The prevalence of atypical depression based on DSM-IV criteria among samples of subjects with major depressive

Atypical depression is the most common form of depression seen in outpatient clinics in psychiatry.

Criteria for atypical depression. *Atypical feature* as a specifier can be applied to major depressive episodes, bipolar disorder when a major depressive episode is the most recent mood episode, or when atypical features predominate during the most recent two years of dysthymic disorder.

According to the DSM-IV, symptoms of depression with atypical features include the following:

- A. Mood reactivity (i.e., mood brightens in response to positive events)

depression.⁸ But even now, very few studies, if any, have proved superior efficacy of SSRIs over MAOIs in atypical depression.⁹

Another reason for the rebirth of interest in the criteria of atypical depression is based on the observation that this specifier has significance that goes beyond different response to antidepressants.

The aim of this article is to examine the epidemiological characteristics, symptoms, association with bipolar disorder, personality and temperament features, biology, and medication response of atypical depression.

disorder or dysthymia has been reported to be around 40 percent.¹⁰⁻¹² Most of the studies have shown the prevalence of atypical depression to be around four times more common in female patients.^{10,13,14}

Research has also supported the early age of onset of symptoms in patients with atypical depression compared to nonatypical depression. Onset of depressive symptoms in teenagers or patients in their early 20s is more likely to be in the form of atypical depression rather than nonatypical depression.^{13,15,16}

TABLE 1. Major differentiating symptoms of atypical and melancholic (part of non atypical) depression

Symptom	Atypical	Melancholic (nonatypical)
Mood reactivity	Mood reactivity present (brightens in response to positive events)	Lack of mood reactivity even temporarily, when something good happens
Weight/appetite	Significant weight gain or increase in appetite	Significant anorexia or weight loss
Sleep	Excessive sleep all through the day	Decreased sleep with early morning awakening
Psychomotor activity	Leadens paralysis (heavy feeling in arms, legs)	Psychomotor retardation or agitation
Personality/thinking	Interpersonal rejection sensitivity not limited to mood episodes	Excessive or inappropriate guilt during mood episodes
Diurnal variation	Depression likely worse in evening (not part of diagnostic criteria)	Depression regularly worse in morning

SYMPTOMS OF ATYPICAL DEPRESSION

As per DSM-IV, diagnosis of atypical depression requires mood reactivity (ability to feel better temporarily in response to positive life event) plus at least two of following: Hyperphagia (gained at least 5 pounds [2kg] or reports of clear appetite increase during the current depressive illness), hypersomnia (sleep 10 hours per day or two or more hours a day than usual), leaden paralysis (feels as if limbs are weighed down or a constant fatigue), and long-standing pattern of rejection sensitivity

(patient frequently has excessive response to rejection, which results in social and/or occupational impairment).

Significantly, depression with atypical feature is a chronic disorder with many subjects describing onset in childhood or adolescences^{13,15,16} and indicating that they have felt this way all of their lives. Posternak and Zimmerman¹⁷ analyzed the individual symptoms of atypical depression and found the severity and chronicity of atypical depression was positively associated with specific symptoms of leaden

paralysis and rejection sensitivity (Table 1).

Demographic and clinical correlates have been found to differ with each of the symptoms of atypical depression. This is thought to occur because atypical depression can be part of different types of mood disorders, such as bipolar disorder, unipolar depression, or dysthymia, with comorbid conditions further influencing the presence of particular symptoms.^{4,10,18}

ASSOCIATION WITH BIPOLAR II DISORDER

Atypical depression and bipolar depression, especially when the latter is bipolar disorder type II, seem to be closely associated. Many studies have found atypical depression as a common part of bipolar disorder¹⁹⁻²⁴ with some reporting it to be the case in two-thirds of the cases,^{10,24,25} though some of these studies included even "soft bipolarity," i.e., antidepressant-induced hypomania, history of <4 days of hypomania (instead of 4 days minimum specified in DSM IV)^{10,24,25} as episodes of hypomania. Atypical depression with early onset (younger than age 20) has been found to be more likely associated with bipolar disorder.²⁶ Genetic vulnerability to bipolar illness is supported by the presence of more positive family history of bipolar disorder in patients with atypical depression than nonatypical depression.^{4,27,28}

Longer duration of illness, frequent episodes, common occurrence of symptoms of leaden paralysis, and hypersomnia are some of the other features shared by people with atypical depression and those with bipolar depression.¹¹

COMORBIDITY AND COURSE OF ILLNESS

Among all subtypes of depression, atypical depression seems to carry most psychiatric

TABLE 2. Shared criteria (DSM-IV) for atypical depression and avoidant personality disorder

Atypical Depression	Avoidant Personality Disorder
Long-standing pattern of interpersonal rejection sensitivity (not limited to mood disorder episodes) resulting in significant functional impairment	Avoidance of activities that involve significant interpersonal contact because of fears of criticism and rejection

Axis 1 comorbidity.^{27,29,30–32} That is why individuals with atypical depression have been reported to suffer more functional impairment, exhibiting much more interpersonal sensitivity, chronic dysphoria, “double depression,” and episodes of affective instability compared to subjects with no atypical depression.^{30,33,34} Benazzi¹⁰ compared the comorbidity in samples of patients with atypical ($n=121$) and nonatypical ($n=133$) depression and found the following ratios: panic disorder/agoraphobia (53.7% vs. 46.6%), obsessive-compulsive disorder (10.7% vs. 9.7%), generalized anxiety disorder (9.9% vs. 5.2%), bulimia nervosa (10.7% vs. 1.5%), and social phobia (8.2% vs. 4.5%). Angst, et al.,¹⁴ came to a similar conclusion, i.e., more comorbid nonaffective disorders in subjects with atypical ($n=59$) compared to nonatypical ($n=52$) depression as follows: panic disorder (17% vs. 8%), all phobias (37% vs. 22%), generalized anxiety (35% vs. 29%), binge eating (27% vs. 10%), social phobia (25% vs. 10%), and drug abuse and dependence (19% vs. 12%). One of the striking findings from this study was the overwhelming association of the ICD-10 diagnosis of neurasthenia (54% vs. 14%) with atypical depression. It has been acknowledged for a long time that there is a relationship between chronic fatigue syndrome and neurasthenia with depression,^{35,36}

but this was the first time the association was linked to a particular subtype of depression. Social phobia as comorbid diagnosis with atypical depression was also found in studies performed by Agosti and Stewart (20%),³³ Alpert, et al. (26%),³⁷ and Perugi, et al. (15%).¹⁸ Angst et al.,¹⁴ compared the suicide attempts in subjects with atypical depression versus nonatypical variants. The results showed 34.6 percent of the patients attempted suicide from the atypical group compared to 20.3 percent from the nonatypical depression group. Similar findings were reported by the national comorbidity survey²⁷ with more suicidal thoughts and attempts, greater disability and restricted activity days, history of more childhood neglect and abuse, and co-occurring psychiatric illness in the subjects with atypical depression.

PERSONALITY AND TEMPERAMENT

Atypical depression is a unique variant of depression that has the personality trait, rejection sensitivity, as part of its diagnostic criteria. DSM-IV requires rejection sensitivity to be present prior to the current depressive episode. Liebowitz and Klien³⁸ thought that personality traits formed the core symptom for atypical depression. Recent literature has associated histrionic, borderline, and avoidant personality disorders with atypical depression.^{20,39,37,40} Posternak and Zimmerman⁴⁰

suggested that the overlap between personality disorders and atypical depression could be an artifact of shared criteria in the diagnoses (Table 2).

Chopre, et al.,⁴¹ used a dimensional approach to clarify the association. Results from this study showed high neuroticism, impulsivity, anger, hostility, and low deliberation as traits common to both atypical depression and cluster B and C personality disorders.

Atypical depression has also been associated with distinct temperament. Cloninger, et al.,⁴² found interesting temperamental differences in subjects with atypical depression. This study reported specific temperament traits in people with atypical depression, which included the tendency to anticipate failure, rumination with high anticipatory worry, difficulty getting over humiliation and embarrassment, giving up easily in frustration, extreme sensitivity to criticism, underachievement (low persistence), and tendency to discuss feelings and experiences (high attachment).

BIOLOGICAL ASPECTS

Atypical depression as a biologically distinct subtype of depression has been suggested by its superior response to MAOIs compared to TCAs and from cerebral laterality, as well from genetic and neuroendocrine studies.⁴³ Atypical depression has been shown to be associated with exaggerated negative feedback regulation of HPA axis.^{44–46} Though nonatypical cases of depression have also been found to be associated with malfunction of hypothalamic pituitary adrenal (HPA) axis, corticotrophin releasing factor (CRF) levels are high rather than low as in subjects with atypical depression.^{47,48} Bruder, et al.,⁴⁹ reported that patients with atypical depression showed right hemisphere dominance for

perceiving chimeric faces. This finding was reported to be unrelated to the subject's gender or any comorbidity and is opposite to left-sided cerebral laterality seen in nonatypical depression.⁴⁹

Genetic predisposition has been found to be different in atypical depression with more family members having chronic atypical depression (many times part of bipolar disorder), less having nonatypical depression, and a comparatively higher concordance in monozygotic twin pairs.^{50,51}

PHARMACOTHERAPY RESPONSE

Patients with atypical depression have been shown to have less or no response to TCAs and better response to MAOIs (Table 3).^{2-5,52}

After their introduction, SSRIs, because of their better efficacy and tolerance and serotonergically mediated effects on mood and appetite, were considered potentially better alternatives than the TCAs or MAOIs. But in 1994, Lonnquist, et al.,⁵³ found meclbemide (an MAOI not available in the US) more effective than fluoxetine (SSRI) in atypical depression, though later, in 1996, Pande, et al.,⁸ found fluoxetine equally effective to phenelzine, an MAOI, in atypical depression. Further, Sogaard, et al.,⁵⁴ in 1999 found meclbemide less effective than sertraline (SSRI). Another study compared fluoxetine, imipramine, and placebo in atypical depression and found fluoxetine and imipramine similarly effective and both superior to placebo.³ One large pharmaceutical study that compared sertraline and imipramine in atypical depression was never published, raising doubts about the results.¹⁶

The influence of serotonin in atypical depression has been seen with the positive therapeutic effects of chromium picolinate (5HT2A downregulation),

especially on carbohydrate craving and appetite regulation⁵⁵ and, in some cases, with the use of gepirone⁵⁶ (5HT1A agonist, not available in US). With other newer antidepressants, Rye, et al.,⁵⁷ have reported a single case of late onset atypical depression responsive to bupropion. An open trial of venlafaxine ($n=17$) in late life atypical depression has also yielded positive results.⁵⁸ Unfortunately, few trials have compared efficacy of MAOIs with SSRIs or other newer

antidepressants, and most of the ones performed (Table 3) had either small patient samples and high risk of significant Type 2 error or used Columbia criteria (not DSM-IV) for atypical depression.^{9,14}

DISCUSSION

The term *atypical* is usually associated with something rare. But atypical depression, though unique in its presentation, is certainly not rare in depressive disorders. Current literature

TABLE 3. Atypical depression patient response to medication

Study	No. of Subjects	Positive Response	Limitations
Lonnqvist, et al. ⁵³ (meclobemide vs fluoxetine)	$n=52$	67% with meclbemide and 55% with fluoxetine	Columbia ¹⁴ criteria,* small sample
Pande, et al. ⁸ (fluoxetine vs phenelzine)	$n=42$	80–85% with both	Columbia criteria, small sample
Sogaard, et al. ⁵⁴ (meclobemide vs sertraline)	$n=197$	77% with sertraline and 67% with meclbemide	Columbia criteria
McGrath, et al. ³ (fluoxetine vs imipramine)	$n=154$	Around 55% in fluoxetine and imipramine	Columbia criteria
McGrath, et al. ⁵⁶ (gepirone)	$n=60$	62%	Columbia criteria, small sample
Roose, et al. ⁵⁸ (venlafaxine)	$n=17$	65–70%	Small sample, mean age 65 yr, open trial
Docherty, et al. ⁵⁵ (chromium picolinate)	$n=113$	65%	Subjects mostly obese, main effect on appetite

* Columbia criteria require mood reactivity and one of the following symptoms: Increased appetite, hypersomnia, leaden paralysis or rejection sensitivity (unlike DSM- IV which requires mood reactivity and two of four symptoms).

supports atypical depression as a subtype of depression with high prevalence, early onset in life, and tendency to persist longer. Early onset of atypical depression might explain the reason TCAs have been relatively ineffective in children.⁵⁹

Patients of atypical depression with chronic course, pattern of long-standing rejection sensitivity, and the always present fatigue can easily end up with primary diagnosis of personality disorder or simply neurosis. This can have profound adverse effects if it results in denial of a trial of antidepressants, which have been found to be very effective.¹²

The chief complaint of fatigue

found 69 percent of patients with bipolar disorder were initially misdiagnosed, with more than one third of cases remaining misdiagnosed for more than 10 years.⁶⁰

It has been acknowledged that patients with atypical depression have shown good response to antidepressants.¹² Though there do not appear to be any large-scale studies that endorse the use of SSRIs over MAOIs as first-line treatment of atypical depression, the potential for serious adverse effects with MAOIs (hypertensive crisis) makes SSRIs an attractive and relatively safe option. But patients unresponsive to SSRIs or other second generation antidepressants should be

4. Rabkin JG, Quitkin FM, McGrath PJ, et al. Should atypical depression be included in DSM IV? In: American Psychiatric Association. *DSM IV Source Book*. Washington, DC: American Psychiatric Press Inc., 1996;2:239–60.
5. McGrath PJ, Stewart JW, Harrison WM, et al. Predictive value of symptoms of atypical depression for differential drug treatment outcome. *J Clin Psychopharmacol* 1992;12:197–202.
6. West ED, Dally PJ. Effects of iproniazid in depressive syndromes. *Br Med J* 1959;15(5136):1491–4.
7. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental disorders, Fourth Edition*. Washington, DC: American Psychiatric Press Inc., 1994.
8. Pande AC, Birkett M, Fechner-Bates S, et al. Fluoxetine versus phenelzine in atypical depression. *Biologic Psychiatry* 1996;40:1017–20.
9. Nierenberg AA, Alpert JE., Pava J, et al. Course and treatment of atypical depression. *J Clin Psychiatry* 1989;59(suppl 18):5–9.
10. Benazzi F. Prevalence of bipolar disorder

Atypical depression is a unique variant of depression that has the personality trait, rejection sensitivity, as part of its diagnostic criteria.

as part of the symptom of leaden paralysis in people with atypical depression can also result in misdiagnosis of chronic fatigue syndrome. That is why patients with no physical signs and symptoms (like tender lymph nodes, sore throat) but with history of long-standing fatigue should be carefully screened for presence of atypical depression.

Atypical depression might not be the absolute marker of bipolar depression. But it does call for using more comprehensive screening tools to rule out bipolar illness. It can help with early diagnosis and prevent prolonged suffering of patients with bipolar disorder who are initially misdiagnosed. In a recent survey, the National Depressive and Manic Depressive Association

provided the option of treatment with MAOIs. Unfortunately, the utility of MAOI in this subtype of depression continues to be not as widely accepted as it should be.

To conclude, it is imperative that the symptoms of atypical depression be recognized so that appropriate treatment can be initiated and patient suffering minimized.

REFERENCES

1. Rosenbaum JF. Depression and its subtypes: A treatment update. *J Clinical Psychiatry* 1998;59(suppl 18):37–8.
2. Quitkin FM, McGrath PJ, Stewart JW, Klein DF. A reappraisal of atypical depression. *Am J Psychiatry* 2003;160:798–800.
3. McGrath PJ, Stewart JW, Janal MN, et al. A placebo-controlled study of fluoxetine versus imipramine in the acute treatment of atypical depression. *Am J Psychiatry* 2000;157:344–50.
4. Rabkin JG, Quitkin FM, McGrath PJ, et al. Should atypical depression be included in DSM IV? In: American Psychiatric Association. *DSM IV Source Book*. Washington, DC: American Psychiatric Press Inc., 1996;2:239–60.
5. McGrath PJ, Stewart JW, Harrison WM, et al. Predictive value of symptoms of atypical depression for differential drug treatment outcome. *J Clin Psychopharmacol* 1992;12:197–202.
6. West ED, Dally PJ. Effects of iproniazid in depressive syndromes. *Br Med J* 1959;15(5136):1491–4.
7. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental disorders, Fourth Edition*. Washington, DC: American Psychiatric Press Inc., 1994.
8. Pande AC, Birkett M, Fechner-Bates S, et al. Fluoxetine versus phenelzine in atypical depression. *Biologic Psychiatry* 1996;40:1017–20.
9. Nierenberg AA, Alpert JE., Pava J, et al. Course and treatment of atypical depression. *J Clin Psychiatry* 1989;59(suppl 18):5–9.
10. Benazzi F. Prevalence of bipolar disorder
11. Akiskal HS, Benazzi F. Atypical depression: A variant of bipolar II or a bridge between unipolar and bipolar II? *J Affect Dis* 2005;84:209–17.
12. Quitkin FM. Depression with atypical features: Diagnostic validity, prevalence, and treatment. Primary Care Companion. *J Clin Psychiatry* 2002;4(3):94–9.
13. Thase ME. Antidepressant treatment of atypical depression. Abstract. San Diego, CA: American Psychiatric Association Annual Meeting, 1997:73B.
14. Angst J, Gamma A, Sellaro R, et al. Toward validation of atypical depression in the community: results of the Zurich cohort study. *J Affect Disord* 2002;72:125–38.
15. Stewart JW, Quitkin FM, McGrath PJ, Klein DF. Defining the boundaries of atypical depression: Evidence from the HPA axis supports course of illness distinctions. *J Affect Disord* 2005;86:161–7.
16. Stewart JW, McGrath PJ, Quitkin FM. Do age of onset and course of illness predict different treatment outcome among DSM IV depressive disorders

- with atypical features?
Neuropsychopharmacology 2002;26:2:237–45.
17. Posternak MA, Zimmerman M. Symptoms of atypical depression. *Psychiatry Res* 2001;104:175–81.
18. Lam RW, Stewart JW. The validity of atypical depression in DSM IV. *Compr Psychiatry* 1996;37:375–83.
19. Benazzi F. Prevalence of bipolar II disorder in atypical depression. *Eur Arch Psychiatry Clin Neurosci* 1999;249:62–5.
20. Perugi G, Akiskal HS, Lattanzi L, Ceconi D, et al. The high prevalence of soft bipolar II features in atypical depression. *Compr Psychiatry* 1998;39(2):63–71.
21. Benazzi F. Prevalence and clinical features of atypical depression in depressed outpatients: A 467-case study. *Psychiatry Res* 1999;86:259–65.
22. Benazzi F. Is atypical depression a moderate severity depression? A 536-case study. *J Psychiatry Neurosci* 2000;25(2):116.
23. Benazzi F. Depression with DSM IV atypical features: a marker for bipolar II disorder. *Eur Arch Psychiatry Clin Neurosci* 2000;250:53–5.
24. Angst J, Gamma A, Benazzi F, Ajdacic V, et al. Toward a redefinition of subthreshold bipolarity: Epidemiology and proposed criteria for bipolar II, minor bipolar disorders and hypomania. *J Affect Disord* 2003;73:133–46.
25. Akiskal HS. The prevalent clinical spectrum of bipolar disorders: Beyond DSM IV. *J Clin Psychopharmacol* 1996;16(suppl 1):4S–14S.
26. Benazzi F. Testing DSM IV definition of atypical depression. *Ann Clin Psychiatry* 2003;15:1:9–16.
27. Matza SL, Revicki DA, Davidson JR, Stewart JW. Depression with atypical features in the national co morbidity survey. *Arch Gen Psychiatry* 2003;60:817–26.
28. Sullivan PF, Kessler RC, Kendler KS. Latent class analysis of life time depressive symptoms in the national comorbidity survey. *Am J Psychiatry* 1998;155:1398–406.
29. Benazzi F. Is there a link between atypical and early onset “unipolar” depression and bipolar disorder? *Compr Psychiatry* 2003;44(2):102–9.
30. Novick JS, Stewart JW, Wisniewski SR, et al. STAR D investigators. Clinical and demographic features of atypical depression in outpatients with major depressive disorder: Preliminary findings from STAR D. *J Clin Psychiatry* 2005;66(8):1002–11.
31. Angst J, Gamma A, Benazzi F, et al. Atypical depressive syndromes in varying definitions. *Eur Arch Psychiatry Clin Neurosci* 2006;256(1):44–54.
32. Benazzi F. Testing atypical depression definitions. *Int J Meth Psychiatry Res* (2005);14:2:82–91.
33. Agosti V, Stewart JW. Atypical and non-atypical subtypes of depression: Comparison of social functioning, symptoms, course of illness, comorbidity and demographic features. *J Affect Dis* 2001;65:75–9.
34. Stewart JW, Rabkin JG, Quitkin FM, et al. Atypical depression. In: Dunner DL (ed). *Current Psychiatric Therapy*. Philadelphia, PA: WB Saunders Company, 1993:215–20.
35. Bennet BK, Hickie IB, Vollmer-Conna US, et al. The relationship between psychological and immunological variables in acute infectious illness. *Aust NZ J. Psychiatry* 1998;32:180–6.
36. Hickie I, Hadzi-Pavlovic D, Ricci C. Reviving the diagnosis of neurasthenia. *Psychol Med* 1997;27:989–94.
37. Alpert KE, Uebelacker LA, McLean NE, et al. Social phobia, avoidant personality disorder, and atypical depression: Co-occurrence and clinical implications. *Psychol Med* 1997;27:627–33.
38. Liebowitz MR, Klien DF. Hysteroid dysphoria. *Psychiatr Clin North Am* 1979;2:555–76.
39. Perugi G, Toni C, Traverso MC, Akiskal HS. The role of cyclothymia in atypical depression: Toward a data-based reconceptualization of the borderline-bipolar II connection. *J Affect Disord* 2003;73:87–98.
40. Posternak MA, Zimmerman M. Partial validation of the atypical features subtype of major depressive disorder. *Arch Gen Psychiatry* 2002;59:70–6.
41. Chopra KK, Bagby M, Dickens S, et al. A dimensional approach to personality in atypical depression. *Psychiatry Res* 2005;134:161–7.
42. Cloninger CR, Svrakie DM, Przybeck TR. A psychobiological model of temperament and character. *Arch Gen Psychiatry* 1993;50:975–90.
43. Posternak MA. Biological markers of atypical depression. *Harv Rev Psychiatry* 2003;11:1:1–7.
44. Levitan RD, Vaccarino FJ, Brown GM, Kennedy SH. Low dose dexamethasone challenge in women with atypical major depression: Pilot study. *J Psychiatry Neurosci* 2002;27:1:47–51.
45. Asnis GM, McGinn LK, Sanderson WC. Atypical depression: Clinical aspects and noradrenergic function. *Am J Psychiatry* 1995;152:31–6.
46. McGinn LK, Asnis GM, Robinson E. Biological and clinical validation of atypical depression. *Psychiatry Res* 1996;60:191–8.
47. Harvard Health Publications. Atypical depression. *Harv Ment Health Lett* 2005;22:3:1–3.
48. Anisman H, Ravindran AV, Griffiths J, Merali Z. Endocrine and cytokine correlates of major depression and dysthymia with typical or atypical features. *Mol Psychiatry* 1999;4:2:182–8.
49. Bruder GE, Stewart JW, McGrath PJ, et al. Atypical depression: Enhanced right hemispheric dominance for perceiving emotional chimeric faces. *J Abnorm Psychol* 2002;111:3:446–54.
50. Kendler KS, Eaves LJ, Walters EE, et al. The identification and validation of distinct depression syndromes in a population based sample of female twins. *Arch Gen Psychiatry* 1996;53:391–9.
51. Stewart JW, McGrath PJ, Rabkin JG, Quitkin FM. Atypical depression: A valid clinical entity? *Psychiatr Clin North Am* 1993;16:479–95.
52. Sotsky SM, Simmens SJ. Pharmacotherapy response and diagnostic validity in atypical depression. *J Affect Dis* 1999;54:237–47.
53. Lonnqvist J, Shivo S, Syvalahti E, Kiviruusu O. Meclobemide and fluoxetine in atypical depression: A double-blind trial. *J Affect Dis* 1994;32:169–77.
54. Sogaard J, Lane R, Latimer P, Behnke K, et al. A 12-week study comparing moclobemide and sertraline in the treatment of outpatients with atypical depression. *J Psychopharmacol* 1999;13:4:406–14.
55. Docherty JP, Sack DA, Roffman M, et al. A double-blind, placebo-controlled, exploratory trial of chromium picolinate in atypical depression: Effect on carbohydrate craving. *J Psychiatr Pract* 2005;11:5:302–14.
56. McGrath PJ, Stewart JW, Quitkin FM, et al. Gepirone treatment of atypical depression: Preliminary evidence of serotonergic involvement. *J Clin Psychopharmacol* 1994;14:347–52.
57. Rye DB, Dihenia B, Biliwise DL. Reversal of atypical depression, sleepiness, and REM-sleep propensity in narcolepsy with bupropion. *Depress Anxiety* 1998;7:92–5.
58. Roose SP, Miyazaki M, Devanand D, et al. An open trial of venlafaxine for the treatment of late life atypical depression. *Int J Geriatr Psychiatry* 2004;19:10:989–94.
59. Geller B, Reising D, Leonard HL, et al. Critical review of tricyclic antidepressants use in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 1999;38:513–16.
60. Hirschfeld RM, Lewis L, Vornik LA. Perceptions and impact of bipolar disorder: How far have we really come? Results of the National Depressive and Manic Depressive Association 2000 survey of individuals with bipolar disorder. *J Clin Psychiatry* 2003;64:161–74. ●